SUMMARY OF SAFETY AND EFFECTIVENESS DATA
FOR A SUPPLEMENTAL PREMARKET APPROVAL APPLICATION

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Excimer Laser System
Device Trade Name:	VISX STAR S4™ Excimer Laser System with Variable Spot Scanning (VSS™) and WaveScan WaveFront® System
Applicant's Name and Address:	VISX, Incorporated 3400 Central Expressway Santa Clara, CA 95051-0703
Date of Panel Recommendation:	None
Premarket Approval (PMA) Application Number:	P930016/S17
Date of Notice of Approval to Applicant:	12/14/2004

The STAR Excimer Laser was originally approved on March 27, 1996, under PMA P930016, for the limited indication for myopic photorefractive keratectomy (PRK) using a 6.0 mm ablation zone in patients 18 years of age or older with 1.0 to 6.0 diopters (D) of myopia with astigmatism of ≤ 1.0 D whose refractive change for one year prior to treatment is within ± 0.5 D.

This clinical indication was expanded in supplements 3 (approved on April 24, 1997), (approved on January 29, 1998), 7 (approved November 2, 1998), and 10 (approved October 18, 2000) to include PRK in patients 21 years of age or older in PRK treatments for the reduction or elimination of myopia (nearsightedness) of between 0 and -12.0 D spherical myopia at the spectacle plane and up to -4.0 D of astigmatism, hyperopia (sphere only) of between +1.0 and +6.0 D spherical equivalent with no more than 1.0 D of refractive astigmatism, and hyperopia between +0.5 and +5.0 D sphere at the spectacle plane with refractive astigmatism from +0.5 to +4.0 D with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D. On November 19, 1999 (P990010), the clinical indication was further expanded to include laser in situ keratomileusis (LASIK) treatments in patients 18 years of age or older for the reduction or elimination of myopia (nearsightedness) from 0 to -14.0 D with or without -0.50 to -5.0 D of astigmatism. Supplement 12 (approved April 27, 2001) expanded the indication to include patients 21 years of age or older in treatments for the reduction or elimination of naturally occurring hyperopia between +0.5 D and +5.0 D sphere at the spectacle plane with or without refractive astigmatism up to +3.0 D with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D. Supplement 14 (approved November 16, 2001) expanded the indication for the reduction or elimination of naturally occurring mixed astigmatism where the magnitude of cylinder (≤ 6.0 D at the spectacle plane) is greater than the magnitude of sphere and the cylinder and sphere have opposite signs. Supplement 15 (approved August 7, 2002) added an auto-centering function to the ActiveTrak™ eye tracking system and changed the trade name to the STAR S4. Supplement 16 (approved May 23, 2003) expanded the clinical indication for wavefront-guided laser assisted in situ keratomileusis (LASIK) for the reduction or elimination of myopic astigmatism up to - 6.00 D MRSE, with cylinder between 0.00 and -3.00 D, in patients 21 years of age or older. Supplement 18 (approved June 7, 2004) upgraded the software to WaveScan Version 3.50.

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The sponsor submitted this supplement to further expand the clinical indications. The updated clinical data to support the expanded indication is provided in this summary. The hazard analysis and software testing preclinical test results supporting this indication were presented in PMA #P930016 supplement 18. Bench test results of the WaveScan WaveFront® System's ability to measure conventional and high order aberrations were presented in PMA #930016 supplement 16. Profilometry validation of ablation patterns for hyperopic astigmatism was included in this supplement. For more information on the data which supported the approved indications, the summaries of safety and effectiveness data (SSED) for P930016 and P990010 should be referenced. Written requests for copies of the SSED can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857 under Docket # 97M-0084 (P930016 and S3), Docket # 99M-0293 (S5), Docket # 00M-1391 (S7), Docket # 01M-0015 (S10), Docket # 01M-0305 (S12), Docket # 01M-0522 (S14), Docket# 03M-0333 (S16), and Docket # 00M-1447 (P990010) or you may download the files from the internet sites http://www.fda.gov/cdrh/pdf/p930016.pdf and http://www.fda.gov/cdrh/pdf/p990010.pdf.

II. INDICATIONS FOR USE

The STAR S4™ Excimer Laser System with Variable Spot Scanning (VSS™) and WaveScan WaveFront® System is indicated for wavefront-guided laser assisted in situ keratomileusis (LASIK):

- for the reduction or elimination of hyperopia and hyperopic astigmatism up to 3.00 D MRSE, with cylinder between 0.00 and 2.00 D;
- in patients 21 years of age or older; and
- in patients with documented evidence of a change in manifest refraction of no more than 1.00 D (in both cylinder and sphere components) for at least one year prior to the date of pre-operative examination.

III. CONTRAINDICATIONS

Laser refractive surgery is contraindicated:

- in patients with collagen vascular, autoimmune or immunodeficiency diseases.
- in pregnant or nursing women.
- in patients with signs of keratoconus or abnormal corneal topography.
- in patients who are taking one or both of the following medications: isotretinoin (Accutane®) or amiodarone hydrochloride (Cordarone®).

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the device labeling.

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V. DEVICE DESCRIPTION

A. WaveScan WaveFront® System

The WaveScan WaveFront System is an integral part of this approval. It is a class III accessory device and has a separate user manual. It is a diagnostic instrument indicated for the automated measurement, analysis, and recording of refractive errors of the eye: including myopia, hyperopia, astigmatism, coma, spherical aberration, trefoil, and other higher order aberrations through sixth order, and for displaying refractive data of the eye to assist in prescribing refractive correction.

The WaveScan WaveFront System measures the refractive error and wavefront aberrations of the human eye using a Hartmann-Shack wavefront sensor. The measurements can be used to determine regular (sphero-cylindrical) refractive errors and irregularities (aberrations) that cause decreased or blurry vision in the human eye.

The function of the Hartmann-Shack sensor is to measure the refractive error of the eye by evaluating the deflection of rays emanating from a small beam of light projected onto the retina. To control the natural accommodation of the eye during WaveScan® imaging, the system incorporates a fogged fixation target.

The WaveScan System optical head projects a beam of light onto the retina. The light reflects back through the optical path of the eye and into the wavefront device. The reflected beam is imaged by a lenslet array onto the charge-coupled device (CCD). Each lens of the array gathers light information (deflection information) from a different region of the pupil to form an image of the light that passes through that region of the pupil. An array of spots are imaged on the CCD sensor. The system compares the locations of the array of spots gathered from the CCD to the theoretical ideal (the ideal plane wave).

The WaveScan System software uses these data to compute the eye's refractive errors and wavefront aberrations using a polynomial expansion. The system displays the refractive errors and wavefront aberrations as the optical path difference (OPD) between the measured outgoing wavefront and the ideal plane wave. The WaveScan system software subtracts the refractive errors from the wavefront errors map and displays the higher order aberrations as OPD errors. Regions of the pupil with positive OPD are in front of the ideal plane wave and areas with negative OPD are behind the ideal plane wave.

1. Data Collection

   The eye of the patient is centered in the instruments field of view and the image of the eye is brought in focus. As the patient fixates on the target, the fogging system is engaged to optically adjust the position of the target beyond the far point of the patient. This forces the patient to relax their accommodative system, so that the refraction of the eye is measured accurately. There is no pharmaceutical eye dilation required for the patient.

2. Wavefront Measurement

   During the data capture, four images are captured from the Hartmann-Shack camera within a short interval of time. The pupil camera of the instrument captures the image of the eye during the same time interval. The spot pattern images are processed to

reconstruct the wavefront and if two or more of them pass the acceptance criteria, the valid measurements are averaged to yield the final measurement for the examination.

3. Registration

   Internal instrument calibration establishes the coordinate transformation between the pupil imaging camera and the Hartmann-Shack camera, so that the wavefront map can be correctly centered at the center of the pupil during the measurement.

4. Treatment Design

   The target treatment shape is automatically calculated by the WaveScan instrument from the wavefront data. Once the target shape is established, VSS™ software module generates the commands for the laser to create the target shape on the cornea. Corneal geometry, represented by the keratometry values, is taken into account in computing the laser instructions.

   CustomVue™ ablations for hyperopic astigmatism are approved for an optical zone of 6.0mm, and a blend zone of 1.5 mm for a total ablation zone of 9 mm. No treatments with optical zones greater than 6.0 mm were attempted in the U.S. Clinical Trial. All treatments utilized a variable repetition rate to a maximum of 20Hz. CustomVue ablations for this PMA are locked out for hyperopic corrections above 5.0 D MRSE and 2.0 D cylinder as measured by manifest refraction.

   The final commercial release versions for CustomVue are WaveScan software version 3.50 together with STAR software version 4.6. The WaveScan software is capable of calculating a hyperopic optical zone up to 6.5 mm with total ablation zone up to 9.5 mm.

5. Data Transfer

   The treatment files produced by the WaveScan® instrument contain information about the patient, such as name, ID and refractive data and the set of instructions for the VISX STAR laser. They are copied onto a floppy disc or portable USB drive for transfer to the laser. The files are encrypted to prevent data tampering or data corruption.

Features and components of the WaveScan WaveFront System include:

- Computer Control
- PC and Monitor
- Isolation Transformer
- Power Supply
- LED
- Optical Head
- Printer
- Motorized table

B. Microkeratome

The LASIK procedure required the use of a commercially available microkeratome that has been cleared for marketing via premarket notification. Three different microkeratomes were used in this study. Each device consisted of a sterilization/storage tray which includes the shaper head, a left/right eye adapter, suction ring, suction handle, blade handling pin, and corneal reference marker. The instrument motor, tonometer, cleaning brush, disposable blades, power/suction supply unit with vacuum and motor footswitches and power cords are provided as separate components in an accessory stand and equipment suitcase which complete the system. Keratomes used in the clinical study included: Advanced Medical Optics, Inc. (AMO) AMADEUS™ Microkeratome, Bausch & Lomb Hansatome® Microkeratome, and Moria M2 Microkeratome.

C. STAR S4™ Excimer Laser System

The STAR S4 laser system is a 193nm excimer laser system that delivers spatially scanning ultraviolet pulses of variable diameters and slits on to the cornea. The range of diameters and slits available during treatments are 0.65mm to 6mm. An auto-centering dual camera infrared eye tracking system (ActiveTrak™), together with the delivery system, compensates for eye movements during laser correction to maximize the corneal reshaping accuracy. An operating microscope is used to observe the patient procedure and to facilitate accurate focus and laser beam alignment. A debris-removal system is designed to evacuate the debris plume that occurs during ablation. The operating chair and fixation LED align the patient, while a video camera and monitor records the patient treatment.

The variable spot scanning (VSS™) feature of the laser, used for CustomVue™ treatments delivers variable diameter ultraviolet pulses to precise locations by the scanning delivery system. The VSS algorithm optimizes the ablation pattern by choosing the best combination of beam diameters and locations to achieve a target shape. VSS expands the laser capability to achieve a broader spectrum of ablation shapes than conventional treatments because the conventional algorithm optimizes only the diameter for myopic treatments and slits for hyperopic treatments.

Conventional STAR treatments utilize sphere, cylinder and axis components which are entered manually into the laser by the operator to generate the ablation treatment. CustomVue™ treatment information is generated on the WaveScan® system and transferred to the STAR S4 Excimer Laser System. The transferred information includes patient information, eye and refraction information, image of the eye, and ablation instructions to the laser for beam diameters and the exact locations of the beam on the cornea. The VISX Treatment Card defines the number and the types of treatments available.

Features and components of the STAR S4 System include:

- Excimer Laser
- Gas Management System
- Laser Beam Delivery System
- Patient Management System

- Computer Control
- VISX Treatment Card

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are currently several other alternatives for the correction of hyperopia with or without astigmatism:

- Automated lamellar keratoplasty (ALK)
- Contact Lenses
- Conventional Laser in-situ keratomileusis (LASIK - based on phoropter refraction)
- Conventional Photorefractive Keratectomy (PRK - based on phoropter refraction)
- Conductive Keratoplasty (CK)
- Radial Keratotomy (RK)
- Spectacles

Each alternative has its own advantages and disadvantages. A prospective patient should fully discuss with his/her care provider these alternatives in order to select the correction method that best meets his/her expectation and lifestyle.

VII. MARKETING HISTORY

The VISX STAR™ Excimer Laser System has been distributed in 58 countries (Argentina, Aruba, Austria, Australia, Belgium, Bolivia, Brazil, Bulgaria, Canada, Chile, China, Colombia, Cyprus, Czech Republic, Dominican Republic, Dubai, Ecuador, Egypt, Finland, France, Germany, Greece, Hong Kong, Hungary, Indonesia, India, Ireland, Israel, Italy, Jamaica, Japan, Korea, Mexico, The Netherlands, New Zealand, Norway, Pakistan, Paraguay, Peru, Philippines, Portugal, Romania, Russia, Russia-Kazakhstan, Saudi Arabia, Singapore, Slovak Republic, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, United Kingdom, the United States, Uruguay, Venezuela and Vietnam). The VISX STAR Excimer Laser System has not been withdrawn from any country or market for reasons of safety or effectiveness.

The WaveScan WaveFront® System has been distributed in approximately 37 countries (Argentina, Aruba, Australia, Austria, Brazil, Bulgaria, Canada, Colombia, Cyprus, Czech Republic, Dominican Republic, Egypt, Finland, France, Germany, India, Indonesia, Ireland, Italy, Japan, Korea, Mexico, The Netherlands, Portugal, Russia, Saudi Arabia, Singapore, Spain, Sweden, Taiwan, Thailand, Turkey, UAE, United Kingdom, the United States, Uruguay and Vietnam). The WaveScan WaveFront System has not been withdrawn from any country or market for reasons of safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse reactions associated with LASIK include: loss of best spectacle corrected visual acuity (BSCVA), worsening of patient complaints such as double vision, sensitivity to bright lights, increased difficulty with night vision, fluctuations in vision, increase in intraocular pressure, corneal haze, secondary surgical intervention, corneal infiltrate or ulcer, corneal epithelial defect, corneal edema, problems associated with the flap including a lost, misplaced or misaligned flap, retinal detachment, and retinal vascular accidents.

Please refer to the complete listing of adverse events and complications observed during the clinical study which are presented on pages 23 and 24 of the clinical study section.

IX. SUMMARY OF PRECLINICAL STUDIES

A. STAR™ Excimer Laser System

For a summary of non-clinical studies (excluding hazard analysis and software testing) for the STAR Excimer Laser System, refer to the SSED of the original PMA #P930016.

B. WaveScan Wavefront® System

1. Hazard Analysis

Hazard Analysis and Software Testing was conducted for the combined use of the WaveScan WaveFront System and the STAR Excimer Laser System. Hazard Analysis includes 3 separate fault tree analyses (FTAs): WaveScan 3.00, Topographer Measurement for Custom Contoured Ablation Patterns Method (C-CAP) Treatments and STAR software 4.60 version with C-CAP and WavePrint treatment. The WaveScan FTA encompasses the process from patient measurement to the generation of treatment table files. The Topographer FTA encompasses the process from patient measurement to treatment printout. The STAR FTA encompasses all previously identified fault and mitigating circumstances identified with any given treatment process. The software test procedures covered all aspects of new software functionality and performance. All test procedures were completed. The Hazard Analysis and software test report indicated no new hazards affecting safety or effectiveness.

2. Testing for Measurement of Refractive Errors of the Eye with WaveScan Wavefront System

A bench top Study for the measurement of total refractive errors of the eye, including myopia, astigmatism, coma, spherical aberrations, trefoil and other higher order aberrations through sixth order, and Software Testing was conducted for the WaveScan WaveFront® System. The test was designed to measure conventional aberrations in a VISX model eye and in 8 phase plates with different combinations of Zernike aberrations. The data from this study indicated the VISX WaveScan WaveFront System provides an adequate and reliable measurement of total refractive errors of the eye, including myopia, astigmatism, coma, spherical aberration, trefoil and other higher order aberration through sixth order.

3. Profilometry of Ablation

As a part of this PMA, VISX validated the accuracy of WaveScan-derived hyperopic astigmatic corrections by performing a variety of test ablations on flat and curved plastic surfaces. The method of compensating for decreased ablation efficiency with corneal eccentricity was validated by comparisons of ablations on curved surfaces with and without the adjustments. All ablations were scanned with a surface profilometer and showed very good agreement to theoretical targets.

X. SUMMARY OF CLINICAL STUDIES

A clinical study of LASIK treatment, with the VISX STAR™ Excimer Laser System witVariable Spot Scanning and WaveScan derived ablation targets for the correction of hyperopia with and without astigmatism, was conducted under IDE G010048. The data from this study is presented as a basis for consideration and approval. Specifically, safety and effectiveness outcomes at 6 months postoperatively were assessed as stability is reached by that time. The IDE study is described in detail as follows:

A. Study Objective

The objective of this clinical investigation was to demonstrate that LASIK treatment with the VISX STAR Excimer Laser System with Variable Spot Scanning and WaveScan derived ablation targets is safe and effective for the correction of hyperopia with and without astigmatism.

B. Study Design

This was a prospective, multi-center, open-label, non-randomized study where the primary control was the preoperative state of the treated eye (i.e., comparison of pretreatment and post-treatment visual parameters in the same eye).

C. Inclusion and Exclusion Criteria

Enrollment in the study on the effect of LASIK treatment with the VISX STAR Excimer Laser System using Variable Spot Scanning technology with WaveScan® derived ablation targets, was limited to those subjects who met the following inclusion criteria in their operative eye(s):

- Male or female subjects of any race, and at least 21 years old at the time of the pre-operative examination.
- Uncorrected distance visual acuity (UCVA) of 20/40 or worse.
- Hyperopia with and without refractive astigmatism: $\leq$ 6.0 D sphere with $\leq$ 5.0 D cylinder; manifest refraction spherical equivalent (MRSE) $\leq$ 6.0 D at the spectacle plane; and MRSE $\geq$ 1.00 D and/or a cylinder component $\geq$ 1.00 D.
- Best spectacle corrected visual acuity (BSCVA) of 20/25 or better.
- Wavefront measurement pupil size $\geq$ 5.0 mm.

- Manifest refraction within ± 0.75D of WaveScan refraction (sphere and cylinder) and no more than 15 degrees of difference between axes for eyes with cylinder greater than 0.50 D.

- Manifest refraction within ± 0.75 D of Cycloplegic refraction (sphere and cylinder) and no more than 15 degrees of difference between axes for eyes with cylinder greater than 0.50 D.

- WaveScan refraction within ± 0.75 D of Cycloplegic refraction (sphere and cylinder) and no more than 15 degrees of difference between axes for eyes with cylinder greater than 0.50 D.

- Pachymetric measurement minus the maximal depth ablated (as described by the VISX software) added to the flap thickness is greater than or equal to 250 microns (i.e., Pachymetry − [Depth of ablation + Flap thickness] ≥ 250 microns).

- Eyes that demonstrated refractive stability confirmed by a change of less than or equal to 1.0 diopter (sphere and cylinder) at an exam at least 12 months prior to the baseline examination.

- Contact lens wearers who removed soft lenses at least 1 week prior and rigid (Gas permeable and PMMA) lenses at least 2 weeks prior to baseline measurements. At that baseline examination, cycloplegic and manifest refractions as well as corneal topography were obtained. If the investigator determined that the topography was within normal limits, surgery was scheduled at least one week after the initial exam, with no contact lens wear permitted prior to the surgery. If on the day of scheduled surgery, for the operative eye, repeat central keratometry readings and manifest refraction spherical equivalents did not differ significantly from the initial exam measurements (by more than 0.50 diopter), surgery proceeded. If the refractive change exceeded this criterion, the surgery was rescheduled after refractive stability was achieved.

- Planned treatment such that the anticipated post-operative keratometry value in any meridian will be ≤ 50 D. Anticipated post-operative keratometry values will be calculated by: a) adding the total amount of pre-operative manifest sphere and cylinder to the power of the keratometry value in the flat meridian (i.e., sphere (D) + cylinder (D) + Flat K), and b) adding the total amount of pre-operative manifest sphere to the power of the keratometry value in the steep meridian, (i.e., sphere (D) + Steep K).

- Subjects willing and capable of returning for follow-up examinations for the duration of the study.

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Female subjects who were pregnant, breast-feeding or intended to become pregnant over the course of the study.

- Subjects whose fellow eye does not meet all inclusion criteria or fall within approved indications for treatment using the VISX STAR Excimer Laser.

- Subjects who used concurrent topical or systemic medications which might impair healing, including but not limited to: antimetabolites, isotretinoin (Accutane®) within 6

months of treatment, and amiodarone hydrochloride (Cordarone®) within 12 months of treatment.

NOTE: The use of topical or systemic corticosteroids, whether chronic or acute, was deemed to adversely affect healing and subjects using such medication were specifically excluded from eligibility.

- Subjects with a history of any of the following medical conditions, or any other condition that could affect wound healing: collagen vascular disease, autoimmune disease, immunodeficiency diseases, ocular herpes zoster or simplex, endocrine disorders (including, but not limited to unstable thyroid disorders and diabetes), lupus, and rheumatoid arthritis.

  NOTE: The presence of diabetes (either type 1 or 2), regardless of disease duration, severity or control, specifically excluded subjects from eligibility.

- Subjects with a history of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, blepharitis, recurrent corneal erosion, dry eye syndrome, neovascularization > 1mm from limbus), clinically significant lens opacity, clinical evidence of trauma (including scarring), at risk for developing strabismus, evidence of glaucoma, or propensity for narrow angle glaucoma in the operative eye(s).

  NOTE: This included any subject with open angle glaucoma, regardless of medication regimen or control. Additionally, any subject with an IOP greater than 21 mm Hg at baseline is specifically excluded from eligibility.

- Subjects with evidence of keratoconus, corneal irregularity, or abnormal videokeratography in either eye.

- Subjects with known sensitivity or inappropriate responsiveness to any of the medications used in the post-operative course.

- Subjects who were participating in any other clinical trial.

D. Study Plan, Patient Assessments, and Efficacy Criteria

- All subjects were expected to return for follow-up examinations at 1 and 7 days, and 1, 3, 6, 9, 12, and 24 months postoperatively.

- Subjects were permitted to have second eyes (fellow eyes) treated at the discretion of the investigator at the same time as the first eye (primary eyes) or after the primary eye treatment.

- In addition, subjects were eligible for retreatment no sooner than 3 months after treatment with submission of appropriate clinical data, planned treatment, and agreement of the medical monitor in advance. To qualify for retreatment, stability of the refractive outcome must have been documented with serial topographies taken at least 4 weeks apart showing less than 1.0 D of corneal power change in the treatment area, or with manifest refractions taken at least 4 weeks apart showing less than 1.0 D of variation in the manifest refraction spherical equivalent.

Refractive retreatments may be performed if the subject met at least one of the following criteria:

- Manifest refractive spherical equivalent of 0.5 D or greater;
- Manifest astigmatism of 0.5 D or more;
- Distance uncorrected visual acuity of 20/32 or worse; or
- Subjective complaints by the patient with treatable cause as determined by the investigator.

At this time, 5 eyes have undergone retreatment in this study.

All study treatments were conducted using a 6mm optical zone and an 9mm ablation zone with intention of full correction to emmetropia.

The objective parameters measured during the study were:

- At 24 hours and 1-week: subjective patient symptoms, UCVA, and anterior segment examination by biomicroscopy. Manifest refraction and BSCVA were also conducted on each patient at the 1-week visit. Adverse events, complications, medications and other clinical findings were also noted.
- At 1 and 3 months: visual acuity (uncorrected, uncorrected near, distance corrected near, and best spectacle corrected), manifest refraction, keratometry, videokeratography, WaveScan® measurement, contrast sensitivity, applanation tonometry, anterior segment examination by biomicroscopy, and a subjective questionnaire. Dim pupil size was also conducted on each patient at the 3-month visit only. Adverse events, complications, medications and other clinical findings were also noted.

Additional objective parameters to be measured during the study were:

- At 6, 9, 12, and 24 months: visual acuity (uncorrected, uncorrected near, distance corrected near, and best spectacle corrected), manifest refraction, keratometry, corneal videokeratography, WaveScan measurement, contrast sensitivity, applanation tonometry, anterior segment examination by biomicroscopy, and a subjective questionnaire. After cycloplegia, a refraction, dilated media and fundoscopic examination were performed. Adverse events, complications, medications, and other clinical findings were noted as appropriate. If 12 and 24-month examinations are necessary, uncorrected near visual acuity, distance corrected near visual acuity, contrast sensitivity, cycloplegic refraction, dilated fundus examination. and a patient questionnaire are required.
- The primary efficacy variables for this study were: improvement of UCVA, predictability of manifest refraction spherical equivalent (MRSE), and refractive stability.

E. Study Period, Investigational Sites, and Demographics

1. Study Period and Investigational Sites

Seventy-four (74) subjects were treated between May 13, 2003 and September 2, 2003. The database for this PMA supplement reflected data collected through June 21, 2004

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and included 144 eyes: 74 first eyes and 70 second eyes. There were 6 investigational sites that provided eligible data for analysis.

2. Demographics

Of the 144 treated eyes, 42% (60/144) were from male subjects and 58% (84/144) were from female subjects. Furthermore, 86% (124/144) were from Caucasians, 1% (2/144) were from African Americans, 0% (0/0) were from Asian/Pacific Islanders, and 13% (18/144) were of other races. The right eye was treated in 51% (74/144) of the cases and the left eye was treated in 49% (70/144) of the cases. The mean age of the subjects treated was 52 years with a range from 21 to 65.

Table 1 presents demographic information for the all eyes treated.

Table 1:
Demographic Information
All Eyes (n=144)

Category	Classification	n	% Eyes
Gender	Male	60	41.7
	Female	84	58.3
Race	Caucasian	124	86.1
	Asian/Pacific Islander	0	0.0
	African American	2	1.4
	American Indian/Aleut Eskimo	0	0.0
	Hispanic	18	12.5
Eyes	Right	74	51.4
	Left	70	48.6
Contact Lens History	None	122	84.7
	Soft	22	15.3
	RGP/PMMA	0	0.0
Age (in Years)	Average	51.7	
	Standard Deviation	± 8.4	
	Minimum	21	
	Maximum	65	

F. Data Analysis and Results

1. Preoperative Characteristics

Table 2a contains a summary of the preoperative manifest refractive error stratified by sphere and cylinder, expressed in plus cylinder notation for all eyes (safety cohort).

Table 2a:
Pre-Operative Refractive Error Stratified by Manifest Sphere and Cylinder
***Safety Cohort* (n=144)**

	Cylinder													
	0 to 0.5 D		**>0.5 to 1 D**		**>1 to 2 D**		**>2 to 3 D**		**>3 to 4 D**		**>4 to 5D**		**Total**	
Sphere	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
>0 to 1D*	13	9.0	9	6.3	8*	5.6	2*	1.4	0	0.0	0	0.0	32	22.2
>1 to 2 D	40	27.8	20	13.9	5	3.5	1	0.7	0	0.0	0	0.0	66	45.8
>2 to 3 D	13	9.0	8	5.6	5	3.5	0	0.0	2	1.4	0	0.0	28	19.4
>3 to 4 D	5	3.5	3	2.1	1	0.7	1	0.7	2	1.4	0	0.0	12	8.3
>4 to 5 D	4	2.8	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	6	4.2
Total	75	52.1	41	28.5	20	13.9	4	2.8	4	2.8	0	0.0	144	100

**Refractions were performed at 8 feet. When adjusted for optical infinity, 4 eyes (2 with pre-operative cylinder >1 to 2 and 2 eyes with pre-operative cylinder >2 to 3) have myopic spherical power (-0.16 D).*

Table 2b lists the preoperative refractive error stratified by manifest spherical equivalent and cylinder for the effectiveness cohort.

Table 2b:
Pre-Operative Refractive Error Stratified by Manifest Spherical Equivalent and Cylinder
***Effectiveness Cohort* (n=136)**

	Cylinder							
	0 to 0.5 D		**>0.5 to 1 D**		**>1 to 2 D**		**Total**	
MRSE	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
>0 to 1 D	12	8.8	3	2.2	4	2.9	19	14.0
>1 to 2 D	41	30.1	18	13.2	8	5.9	67	49.3
>2 to 3 D	13	9.6	16	11.8	2	1.5	31	22.8
>3 to 4 D	3	2.2	1	0.7	5	3.7	9	6.6
>4 to 5 D	6	4.4	3	2.2	1	0.7	10	7.4
Total	75	55.1	41	30.1	20	14.7	136	100

2. Postoperative Results

a. Patient Accountability

During the study, accountability was excellent. Of the 144 eyes treated, over 95% accountability was achieved at 1, 3 and 6-months.

Tables 3a and 3b present subject accountability over time.

Table 3a:
Subject Accountability
Safety Cohort: All Eyes, n=144

	1 Month		3 Months		6 Months		9 Months		12 Months	
	n	%	n	%	n	%	n	%	n	%
Available for Analysis	142	98.6	142	98.6	137	95.1	124	86.1	27	18.8
Discontinued	0	0.0	0	0.0	1	0.7	6	4.2	6	4.2
Missed Visit	2	1.4	2	1.4	4	2.8	10	6.9	0	0.0
Not yet eligible	0	0.0	0	0.0	0	0.0	0	0.0	107	74.3
Lost to Follow-Up	0	0.0	0	0.0	2	1.4	4	2.8	4	2.8
% Accountability*	**98.6%**		**98.6%**		**95.8%**		**89.9%**		**87.1%**	

*% Accountability=[Available for Analysis/(enrolled-discontinued-not yet eligible)] x 100

Table 3b:
Subject Accountability:
Effectiveness Cohort: All Eyes, n=136

	1 Month		3 Months		6 Months		9 Months		12 Months	
	n	%	n	%	n	%	n	%	n	%
Available for Analysis	134	98.5	134	98.5	131	96.3	118	86.8	27	19.9
Discontinued	0	0.0	0	0.0	1	0.7	6	4.4	6	4.4
Missed Visit	2	1.5	2	1.5	2	1.5	8	5.9	0	0.0
Not yet eligible	0	0.0	0	0.0	0	0.0	0	0.0	99	72.8
Lost to Follow-Up	0	0.0	0	0.0	2	1.5	4	2.9	4	2.9
% Accountability*	**98.5%**		**98.5%**		**97.0%**		**90.8%**		**87.1%**	

*% Accountability=[Available for Analysis/(enrolled-discontinued-not yet eligible)] x 100

b. Stability of Outcome

Eyes with exams at 1, 3, 6 and 9 months post-operatively (n=118). Over 98% of eyes experienced a change in MRSE of ≤ 1.00 D between the 3 and 6-month visit and the 6 and 9-month visit. Refractive stability is reached at 6 months and confirmed at 9-months.

Table 4 presents refractive stability of eyes with visits at 1, 3, 6 and 9 months post-operatively.

Table 4:

Refractive Stability (Eyes that underwent 1, 3, 6, and 9-month visits)

Effectiveness Cohort: All Eyes, n=118

	Between 1 and 3 Months	**Between 3 and 6 Months**	**Between 6 and 9 Months**
Change in MRSE by ≤ 1.0 D	114	116	116
%	96.6	98.3	98.3
95% CI %	(91.5, 99.1)	(94.0, 99.8)	(94.0, 99.8)
Mean Change in MRSE	0.06	0.12	0.01
SD	0.38	0.36	0.31
95% CI	(-0.010, 0.129)	(0.056, 0.184)	(-0.046, 0.067)

c. Effectiveness Outcomes

While 148 eyes were enrolled in this study, only 144 received laser treatment. Two subjects (four eyes) did not receive laser treatment because both experienced an adverse event during creation of the LASIK flap in their primary eye. Though scheduled, treatment to their fellow eye was aborted. Both subjects were followed until resolution.

While all study treatments included an astigmatic correction as diagnosed by the WaveScan device, this was not always reflected in the patient's manifest refraction. Therefore, three tables based solely on manifest refraction are presented for each analysis (all eyes, spherical eyes, and astigmatic eyes).

At this time, 5 eyes have undergone retreatment in this study.

Cohort	**Description**	**N**
Safety	All eyes treated in the study	144
1. Spherical hyperopia	Eyes in *Safety Cohort* with a pre-operative manifest cylinder $\leq$ 0.5 D	75
2. Hyperopic astigmatism	Eyes in *Safety Cohort* with a pre-operative manifest cylinder > 0.5 D	69
3. Effectiveness	Eyes with $\leq$ 2.0 D manifest cylinder	136
• Spherical hyperopia	Eyes in *Effectiveness Cohort* with a pre-operative manifest cylinder $\leq$ 0.5 D	75
• Hyperopic astigmatism	Eyes in *Effectiveness Cohort* with a pre-operative manifest cylinder > 0.5 D	61
➢ Vector & Residual Astigmatic Error Analyses	Astigmatic eyes in *Effectiveness Cohort* with data at point of stability (6-months)	57

1) Uncorrected Visual Acuity (UCVA)

All eyes were targeted for emmetropia. The uncorrected visual acuity results presented in Table 5 exceed the target outcome for UCVA of 20/40 or better (85%) at 1 month and are maintained through 9-months.

Table 5:
UCVA Over Time
Effectiveness Cohort: All Eyes, n=136

	Pre-Op (n=136)	**1 Month (n=134)**	**3 Months (n=134)**	**6 Months (n=131)**	**9 Months (n=118)**	**12 Months (n=27)**
	n % (95% CI)	**n % (95% CI)**	**n % (95% CI)**	**n % (95% CI)**	**n % (95% CI)**	**n % (95% CI)**
20/16 or better	0 0.0 (0.0, 2.2)	19 14.2 (8.8, 21.3)	27 20.1 (13.7, 27.9)	26 19.8 (13.4, 27.7)	28 23.7 (16.4, 32.4)	8 29.6 (13.8, 50.2)
20/20 or better	0 0.0 (0.0, 2.2)	78 58.2 (49.4, 66.7)	80 59.7 (50.9, 68.1)	81 61.8 (52.9, 70.2)	85 72.0 (63.0, 79.9)	21 77.8 (57.7, 91.4)
20/25 or better	0 0.0 (0.0, 2.2)	107 79.9 (72.1, 86.3)	112 83.6 (76.2, 89.4)	104 79.4 (71.4, 86.0)	103 87.3 (79.9, 92.7)	24 88.9 (70.8, 97.6)
20/32 or better	0 0.0 (0.0, 2.2)	119 88.8 (82.2, 93.6)	124 92.5 (86.7, 96.4)	118 90.1 (83.6, 94.6)	111 94.1 (88.2, 97.6)	25 92.6 (75.7, 99.1)
20/40 or better	9 6.6 (3.1, 12.2)	129 96.3 (91.5, 98.8)	130 97.0 (92.5, 99.2)	125 95.4 (90.3, 98.3)	112 94.9 (89.3, 98.1)	25 92.6 (75.7, 99.1)
20/80 or better	68 50.0 (41.3, 58.7)	134 100 (97.8, 100)	134 100 (97.8, 100)	131 100 (97.7, 100)	118 100 (97.5, 100)	27 100 (89.5, 100)
20/200 or better	126 92.6 (86.9, 96.4)	134 100 (97.8, 100)	134 100 (97.8, 100)	131 100 (97.7, 100)	118 100 (97.5, 100)	27 100 (89.5, 100)
Worse than 20/200	10 7.4 (3.6, 13.1)	0 0.0 (0.0, 2.2)	0 0.0 (0.0, 2.2)	0 0.0 (0.0, 2.3)	0 0.0 (0.0, 2.5)	0 0.0 (0.0, 10.5)
Total	136 100	134 100	134 100	131 100	118 100	27 100

2) Accuracy

At 6 months post-operatively, 58.0% (76/131) of eyes were within 0.5 D and 88.5% (116/131) were within 1.0 D of attempted sphere correction. For those eyes in the astigmatic cohort (pre-op manifest refraction cylinder >0.5 D), 68.4% (39/57) were within 0.50 D and 94.7% (54/57) were within 1.0 D of attempted cylinder correction at 6 months post-operatively. Table 6a presents the accuracy of sphere and cylinder over time.

Table 6a:
Accuracy of Sphere (to Zero) and Cylinder (to Zero) Component
***Effectiveness Cohort: All Eyes* (n=136)**

	Pre-Op	**1 Month**	**3 Months**	**6 Months**	**9 Months**	**12 Months**
	N %	**n %**	**n %**	**n %**	**n %**	**n %**
	(95% CI)	**(95% CI)**	**(95% CI)**	**(95% CI)**	**(95% CI)**	**(95% CI)**
Sphere	**n=136**	**n=134**	**n=134**	**n=131**	**n=118**	**n=27**
± 0.50 D	8 5.9 (2.6, 11.3)	71 53.0 (44.2, 61.7)	74 55.2 (46.4, 63.8)	76 58.0 (49.1, 66.6)	79 66.9 (57.7, 75.3)	19 70.4 (49.8, 86.2)
± 1.00 D	30 22.1 (15.4, 30.0)	118 88.1 (81.3, 93.0)	123 91.8 (85.8, 95.8)	116 88.5 (81.8, 93.4)	108 91.5 (85.0, 95.9)	25 92.6 (75.7, 99.1)
Mean ± SD	1.67 ± 1.00	-0.45 ± 0.63	-0.37 ±0.58	-0.28 ± 0.64	-0.28 ±0.58	-0.48 ± 0.47
Attempted		1.67	1.67	1.66	1.71	1.38
Achieved		2.11	2.04	1.94	1.99	1.86
% Achieved		144%	131%	133%	127%	139%
Cylinder*	**n=61**	**n=59**	**n=59**	**n=57**	**n=53**	**n=9**
± 0.50 D	0 0.0 (0.0, 4.8)	45 76.3 (63.4, 86.4)	48 81.4 (69.1, 90.3)	39 68.4 (54.8, 80.1)	40 75.5 (61.7, 86.2)	5 55.6 (21.2, 86.3)
± 1.00 D	41 67.2 (54.0, 78.7)	57 96.6 (88.3, 99.6)	56 94.9 (85.9, 98.9)	54 94.7 (85.4, 98.9)	51 96.2 (87.0, 99.5)	9 100 (71.7, 100)
Mean ± SD	1.08 ± 0.36	0.42 ± 0.37	0.36 ± 0.36	0.44 ± 0.40	0.40 ± 0.36	0.58 ± 0.25
Attempted		1.09	1.09	1.09	1.10	0.92
Achieved		0.66	0.72	0.65	0.70	0.33
% Achieved		59.4%	65.2%	58.4%	62.5%	32.0%

*Analysis of cylinder is limited to those eyes with a pre-operative manifest cylinder >0.5 (n=61).

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At 6 months post-operatively, 65.0% (85/131) of eyes were within ± 0.5 D, and 91% (119/131) were within ± 1.0 D of attempted MRSE correction. Table 6b presents the accuracy of MRSE over time.

Table 6b:
Accuracy of Manifest Refraction Spherical Equivalent Attempted vs. Achieved
Effectiveness Cohort: All Eyes
(N=136)

	Pre-Op (n=136)	**1 Month (n=134)**	**3 Months (n=134)**	**6 Months (n=131)**	**9 Months (n=118)**	**12 Months (n=27)**
	n % (95% CI)	**n % (95% CI)**	**n % (95% CI)**	**n % (95% CI)**	**n % (95% CI)**	**n % (95% CI)**
MRSE						
± 0.50 D	1 0.7 (0.0, 4.0)	73 54.5 (45.7, 63.1)	80 59.7 (50.9, 68.1)	85 64.9 (56.1, 73.0)	91 77.1 (68.5, 84.3)	22 81.5 (61.9, 93.7)
± 1.00 D	19 14.0 (8.6, 21.0)	120 89.6 (83.1, 94.2)	125 93.3 (87.6, 96.9)	119 90.8 (84.5, 95.2)	108 91.5 (85.0, 95.9)	25 92.6 (75.7, 99.1)
± 2.00 D	86 63.2 (54.5, 71.3)	133 99.3 (95.9, 100)	133 99.3 (95.9, 100)	130 99.2 (95.8, 100)	118 100 (97.5, 100)	27 100 (89.5, 100)
Not Reported	0	0	0	0	0	0
Overcorrected			**(Myopic)**			
< -1.00 D		10 7.5 (3.6, 13.3)	6 4.5 (1.7, 9.5)	6 4.6 (1.7, 9.7)	4 3.4 (0.9, 8.5)	2 7.4 (0.9, 24.3)
< -2.00 D		1 0.7 (0.0, 4.1)	1 0.7 (0.0, 4.1)	1 0.8 (0.0, 4.2)	0 0.0 (0.0, 2.5)	0 0.0 (0.0, 10.5)
Undercorrected			**(Hyperopic)**			
> +1.00		4 3.0 (0.8, 7.5)	3 2.2 (0.5, 6.4)	6 4.6 (1.7, 9.7)	6 5.1 (1.9, 10.7)	0 0.0 (0.0, 10.5)
> +2.00		0 0.0 (0.0, 2.2)	0 0.0 (0.0, 2.2)	0 0.0 (0.0, 2.3)	0 0.0 (0.0, 2.5)	0 0.0 (0.0, 10.5)

3) Summary of Key Safety and Effectiveness Variables

Summaries of the key safety and effectiveness variables at Stability Endpoint of 6 Months and stratified by pre-operative MRSE are presented in Tables 7(a-c). All FDA targets were exceeded at this visit.

Table 7a:
Summary of Key Safety and Effectiveness Variables at Stability Endpoint of 6 Months (Stratified by Pre-Operative MRSE)
All Eyes (n=137)

Criteria	0.0 to 1.0 n/N, %		>1.0 to 2.0 n/N, %		>2.0 to 3.0 n/N, %		>3.0 to 4.0 n/N, %		>4.0 to 5.0 n/N, %		>5.0 to 6.0 n/N, %		Cum Total n/N, %	
Effectiveness Variables														
N=131	**n=19**		**n=63**		**n=30**		**n=9**		**n=10**		**n=0**		**N=131**	
UCVA 20/20 or better	15	78.9	41	65.1	16	53.3	6	66.7	3	30.0	0	0.0	81	61.8
UCVA 20/40 or better	19	100	60	95.2	28	93.3	9	100	9	90.0	0	0.0	125	95.4
MRSE ± 0.50 D	14	73.7	44	69.8	17	56.7	5	55.6	5	50.0	0	0.0	85	64.9
MRSE ± 1.00 D	18	94.7	58	92.1	28	93.3	8	88.9	7	70.0	0	0.0	119	90.8
MRSE ± 2.00 D	19	100	63	100	29	96.7	9	100	10	100	0	0.0	130	99.2
Safety Variables														
N=137	**n=19**		**n=65**		**n=31**		**n=10**		**n=12**		**n=0**		**n=137**	
Loss of ≥ 2 lines BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Loss of > 2 lines BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
BSCVA worse than 20/25	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
BSCVA worse than 20/40	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
N=74	**n=12**		**n=40**		**n=13**		**n=3**		**n=6**		**n=0**		**N=74**	
Increase > 2 D cylinder^	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

^For eyes treated with spherical hyperopia

Table 7b:

Summary of Key Safety and Effectiveness Variables at Stability Endpoint of 6 Months (Stratified by Pre-Operative MRSE)

***Eyes with Spherical Hyperopia (by manifest)* n=74**

Criteria	>0.0 to 1.0 n/N, %		>1.0 to 2.0 n/N, %		>2.0 to 3.0 n/N, %		>3.0 to 4.0 n/N, %		>4.0 to 5.0 n/N, %		>5.0 to 6.0 n/N, %		Cum Total n/N, %	
Effectiveness Variables														
N=74	**n=12**		**n=40**		**n=13**		**n=3**		**n=6**		**n=0**		**N=74**	
UCVA 20/20 or better	10	83.3	26	65.0	8	61.5	3	100	2	33.3	0	0.0	49	66.2
UCVA 20/40 or better	12	100	39	97.5	13	100	3	100	5	83.3	0	0.0	72	97.3
MRSE ± 0.50 D	10	83.3	28	70.0	7	53.8	2	66.7	5	83.3	0	0.0	52	70.3
MRSE ± 1.00 D	12	100	37	92.5	13	100	3	100	5	83.3	0	0.0	70	94.6
MRSE ± 2.00 D	12	100	40	100	13	100	3	100	6	100	0	0.0	74	100
Safety Variables														
N=74	**n=12**		**n=40**		**n=13**		**n=3**		**n=6**		**n=0**		**N=74**	
Loss of ≥ 2 lines BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Loss of > 2 lines BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
BSCVA worse than 20/25	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
BSCVA worse than 20/40	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
N=74	**n=12**		**n=40**		**n=13**		**n=3**		**n=6**		**n=0**		**N=74**	
Increase > 2 D cylinder^	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

^For eyes treated with spherical hyperopia

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Table 7c:

Summary of Key Safety and Effectiveness Variables at Stability Endpoint of 6 Months (Stratified by Pre-Operative MRSE)

***Eyes with Hyperopic Astigmatism (by manifest)* n=63**

Criteria	>0.0 to 1.0 n/N, %		>1.0 to 2.0 n/N, %		>2.0 to 3.0 n/N, %		>3.0 to 4.0 n/N, %		>4.0 to 5.0 n/N, %		>5.0 to 6.0 n/N, %		Cum Total n/N, %	
Effectiveness Variables														
N=57	**n=7**		**n=23**		**n=17**		**n=6**		**n=4**		**n=0**		**N=57**	
UCVA 20/20 or better	5	71.4	15	65.2	8	47.1	3	50.0	1	25.0	0	0.0	32	56.1
UCVA 20/40 or better	7	100	21	91.3	15	88.2	6	100	4	100	0	0.0	53	93.0
MRSE ± 0.50 D	4	57.1	16	69.6	10	58.8	3	50.0	0	0.0	0	0.0	33	57.9
MRSE ± 1.00 D	6	85.7	21	91.3	15	88.2	5	83.3	2	50.0	0	0.0	49	86.0
MRSE ± 2.00 D	7	100	23	100	16	94.1	6	100	4	100	0	0.0	56	98.2
Safety Variables														
N=63	**n=7**		**n=25**		**n=18**		**n=7**		**n=6**		**n=0**		**N=63**	
Loss of ≥ 2 lines BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Loss of > 2 lines BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
BSCVA worse than 20/25	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
BSCVA worse than 20/40	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

d. Higher Order Aberrations

Although the WaveScan WaveFront® System measures the refractive error and wavefront aberrations of the human eyes, including myopia, hyperopia, astigmatism, coma, spherical aberration, trefoil, and other higher order aberrations through sixth order, in the clinical study for this PMA, the average higher order aberration did not decrease after CustomVue™ treatment.

e. Safety Outcomes

Adverse Events are reported in Table 8 and Complications in Table 9. Overall, the device was deemed reasonably safe. The benchmark for each adverse event is a rate of less than 1 % per type of event.

Table 8:
Summary of Adverse Events for Hyperopic Astigmatism Study
All Eyes (n=144)

	<1 Month (n=144)		**1 Month (n=142)**		**3 Months (n=142)**		**6 Months (n=137)**		**9 Months (n=124)**		**12 Months (n=27)**	
	n	%	n	%	n	%	n	%	n	%	n	%
Corneal Infiltrate/Ulcer	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Corneal epithelial defect involving the keratectomy at 1 month or later	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Corneal edema at 1 month or later (specify "flap" or "bed" or both)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Epithelium in the interface with loss of 2 or more lines of BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Miscreated Flap	2^	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Melting of the flap (LASIK only)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Uncontrolled IOP >10 mm Hg or any reading > 25 mm Hg	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Late onset of haze beyond 6 months with loss of 2 lines (10 letters) or more BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Decrease in BSCVA of > 10 letter not due to irregular astigmatism as shown by hard contact lens refraction, at 6 months or later	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal Detachment	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal Vascular Accidents	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

^ Because no laser treatment was applied, the data from these 2 eyes were removed from all analyses.

Other: One eye of one subject developed diffuse lamellar keratitis (DLK) prior to the one-month visit, which resolved within six days of onset with no loss of vision.

Table 9:

Summary of Complications for Hyperopic Astigmatism Study

All Eyes (n=144)

	<1 Month (n=144)		**1 Month (n=142)**		**3 Months (n=142)**		**6 Months (n=137)**		**9 Months (n=124)**		**12 Months (n=27)**	
	n	%	n	%	n	%	n	%	n	%	n	%
Misaligned flap	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Corneal edema between 1 week and 1 month after the procedure	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Peripheral corneal epithelial defect at 1 month or later	3	2.1	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
Epithelium in the interface	3	2.1	2	1.4	1	0.7	1	0.7	1	0.8	0	0.0
Foreign body sensation at 1 month or later	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0
Pain at 1 month or later	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Diplopia (ghost images) in the operative eye	0	0.0	16	11.3	10	7.1	11	8.0	8	6.5	0	0.0

Table 10 presents the results of the contrast sensitivity analysis pre-operatively and at 1, 3, and 6-months post-operatively.

Table 10:
Contrast Sensitivity
Safety Cohort: All Eyes (n=144)

	Pre-Op				**Change from Pre-Op to 1 Month**				**Change from Pre-Op to 3 Months**				**Change from Pre-Op to 6 Months**			
CPD	**3**	**6**	**12**	**18**	**3**	**6**	**12**	**18**	**3**	**6**	**12**	**18**	**3**	**6**	**12**	**18**
Dim w/ Glare	**n=144**				**n=139^**				**n=142**				**n=133^**			
Mean	1.52	1.51	1.01	0.57	-0.04	-0.12	-0.16	-0.11	-0.05	-0.12	-0.11	-0.10	-0.03	-0.04	-0.12	-0.06
(SE)	0.02	0.03	0.03	0.03	0.03	0.03	0.04	0.04	0.02	0.03	0.04	0.04	0.02	0.03	0.04	0.04
P Value*					0.09	0.00	0.00	0.00	0.04	0.00	0.00	0.01	0.20	0.21	0.00	0.11
Dim w/o Glare	**n=144**				**n=139^**				**n=142**				**n=133^**			
Mean	1.56	1.63	1.19	0.70	0.00	-0.05	-0.15	-0.10	-0.03	-0.05	-0.14	-0.08	-0.02	-0.03	-0.13	-0.06
(SE)	0.02	0.02	0.03	0.03	0.03	0.03	0.04	0.04	0.02	0.03	0.04	0.04	0.02	0.03	0.04	0.03
P Value* ≤					0.99	0.05	0.00	0.01	0.27	0.08	0.00	0.03	0.44	0.21	0.00	0.04
Bright w/o Glare	**n=144**				**n=139^**				**n=142**				**n=133^**			
Mean	1.73	1.94	1.60	1.13	-0.02	-0.06	-0.10	-0.09	-0.01	-0.01	-0.03	-0.04	0.00	-0.02	-0.03	-0.03
(SE)	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
P Value* ≤					0.20	0.00	0.00	0.00	0.32	0.59	0.15	0.07	0.78	0.26	0.12	0.25

*Two tailed paired t test for the means.
^3 eyes at the 1-month visit and 4 eyes at the 6-month visit did not undergo contrast sensitivity testing

Table 11 shows the percent and number of eyes with changes (>.30 at 2 or more spatial frequencies) in contrast sensitivity at 3 and 6-months.

Table 11:
Change in Contrast Sensitivity
Safety Cohort: All Eyes (n=144)

	3 Months (N=142)			6 Months (N=133*)		
	Decrease	**No Change**	**Increase**	**Decrease**	**No Change**	**Increase**
Bright without Glare	12	125	5	6	123	4
%	8.5	88.0	3.5	4.5	92.5	3.0
Dim without Glare	39	87	16	29	90	14
%	27.5	61.3	11.3	21.8	67.7	10.5
Dim with Glare	48	79	15	36	79	18
%	33.8	55.6	10.6	27.1	59.4	13.5

* Four (4) eyes did not undergo contract sensitivity testing at 6-momth visit.

f. Retreatment

Five (5) eyes had undergone retreatment in this study.

g. Factors Associated with Outcomes

To evaluate the consistency of results and effect of treatment by study site and baseline characteristics, results at 6 months post-operatively were analyzed. The key safety and effectiveness variables were compared to FDA target percentages to determine if the results were significantly different.

No eye had a BSCVA loss of > 2 lines and no eye had a BSCVA worse than 20/40, so there were no detectable differences between study sites and baseline characteristics relative to safety outcomes.

For each effectiveness criterion, comparisons between the actual and target outcomes (MRSE ± 0.50, MRSE ± 1.00, UCVA 20/40 or better) were made using a chi-square goodness-of-fit test. A Mantel-Haenszel one degree of freedom chi-square test was used to compare the observed percentages across categories. Those p-values are used to identify situations where there are differences between categories.

Specifically, the analyses of effect included: sex (female and male), race (white and other), investigational site (1, 2, 4, 5, 6, and 9), age group (<30, 30 to 39, 40 to 49, and ≥ 50), pre-operative contact lens use (None and Soft), pre-operative MRSE (< 2, 2 to <3, 3 to < 4, 4 to <5, and ≥ 5), laser room temperature (< 70°, 70°, 71°, 72° to 73°, 74°, and ≥ 75°), laser room humidity (< 30%, 30% to 35%, 36% to 40%, 41% to 45%, and > 45%), and surgeon.

In these analyses, statistically significant differences in outcomes were identified by comparing actual outcomes with FDA target values (MRSE ± 0.50 / 50%, MRSE ± 1.00 / 75%, UCVA 20/40 or better / 85%).

Throughout these analyses, there were eight instances where the observed value did not meet the FDA target value. For the outcome measure MRSE ± 0.50 D (target=50%), site #1 and site #9 did not meet the target value. Site #1 had an observed value of 38%. At this center, the principal investigator (Dr. Culbertson) had an observed value of 40% and the sub-investigator (Dr. Yoo) had an observed value of 36%. Site #9 had an observed value of 33%; at this site, there is only one investigator (Dr. Maloney). When evaluating the same outcome measure of MRSE ± 0.50 D with laser room temperature, those eyes treated at a center where the laser room temperature was ≥ 75° had an observed value of 38%. For the outcome measure of MRSE ± 1.00 D (target =75%), Dr. Culbertson of site #1 had an observed value of 70%. None of these eight values was statistically significantly different from the target value.

All other subcategories met or exceeded the target value. Indeed, in many of these subcategories, the observed value was statistically significantly superior ($p < 0.05$) to the target value.

h. Patient Satisfaction

Patients were asked to complete a questionnaire for each eye to evaluate vision pre-operatively and post-operatively. Upon completion of the questionnaire, both the patient and the investigator reviewed the form. To be included in the analysis, a pre-operative questionnaire had to have been completed. Patient questionnaire responses are presented pre-operatively and at 3 and 6 months post-operatively. Tables 12a and 12b present a summary of patient satisfaction and patient symptoms.

Table 12a:
Summary of Patient Satisfaction
Effectiveness Cohort: All Eyes (n=136)

	Very Satisfied			Satisfied			Not Sure			Somewhat Dissatisfied			Very Dissatisfied			Not Reported		
	Pre	3M	6M	Pre	3M	6M	Pre	3M	6M	Pre	3M	6M	Pre	3M	6M	Pre	3M	6M
	n=136	n=134	n=131	n=136	n=134	n=131	n=136	n=134	n=131	n=136	n=134	n=131	n=136	n=134	n=131	n=136	n=134	n=131
	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n
	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%
Sharpness and Clarity	26	51	55	64	58	44	6	6	11	29	14	10	11	5	8	0	0	0
	19.1	38.1	43.3	47.1	43.3	34.4	4.4	4.5	8.6	21.3	10.4	7.8	8.1	3.7	6.3	0.0	0.0	0.0
Consistency of Vision	27	39	44	67	62	51	14	14	8	16	16	23	12	3	2	0	0	0
	19.9	29.1	34.4	49.3	46.3	39.8	10.3	10.4	6.3	11.8	11.9	18.0	8.8	2.2	1.6	0.0	0.0	0.0
Daylight Vision	32	59	59	75	62	55	8	5	5	15	5	5	6	3	4	0	0	0
	23.5	44.0	46.1	55.1	46.3	43.0	5.9	3.7	3.9	11.0	3.7	3.9	4.4	2.2	3.1	0.0	0.0	0.0
Night Vision	10	34	43	57	75	51	14	10	14	40	12	15	15	3	5	0	0	0
	7.4	25.4	33.6	41.9	56.0	39.8	10.3	7.5	10.9	29.4	9.0	11.7	11.0	2.2	3.9	0.0	0.0	0.0
Night Vision with Glare	6	28	29	40	64	55	28	17	19	46	22	22	15	3	3	1	0	0
	4.4	20.9	22.7	29.6	47.8	43.0	20.7	12.7	14.8	34.1	16.4	17.2	11.1	2.2	2.3	0.7	0.0	0.0

Table 12b:
Summary of Patient Symptoms
Effectiveness Cohort: All Eyes (n=136)

	Never			Rarely			Sometimes			Often			Always			Not Reported		
	Pre n=136	3M n=134	6M n=131	Pre n=136	3M n=134	6M n=131	Pre n=136	3M n=134	6M n=131	Pre n=136	3M n=134	6M n=131	Pre n=136	3M n=134	6M n=131	Pre n=136	3M n=134	6M n=131
	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n
	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%
Dryness	44	16	18	48	40	30	36	62	58	7	12	17	1	4	5	0	0	0
	32.4	11.9	14.1	35.3	29.9	23.4	26.5	46.3	45.3	5.1	9.0	13.3	0.7	3.0	3.9	0.0	0.0	0.0
Blurry Vision	42	16	19	33	40	44	52	68	52	7	8	6	2	2	7	0	0	0
	30.9	11.9	14.8	24.3	29.9	34.4	38.2	50.7	40.6	5.1	6.0	4.7	1.5	1.5	5.5	0.0	0.0	0.0
Fluctuation of vision	46	15	24	41	55	45	41	50	41	7	12	13	1	2	5	0	0	0
	33.8	11.2	18.8	30.1	41.0	35.2	30.1	37.3	32.0	5.1	9.0	10.2	0.7	1.5	3.9	0.0	0.0	0.0
Glare	25	35	27	49	52	58	49	27	32	13	20	11	0	0	0	0	0	0
	18.4	26.1	21.1	36.0	38.8	45.3	36.0	20.1	25.0	9.6	14.9	8.6	0.0	0.0	0.0	0.0	0.0	0.0
Halos Around Lights	67	56	65	33	39	26	29	19	24	7	14	9	0	6	4	0	0	0
	49.3	41.8	50.8	24.3	29.1	20.3	21.3	14.2	18.8	5.1	10.4	7.0	0.0	4.5	3.1	0.0	0.0	0.0
Difficulty at Night W/Glare	29	41	41	29	41	39	57	35	34	20	17	10	1	0	4	0	0	0
	21.3	30.6	32.0	21.3	30.6	30.5	41.9	26.1	26.6	14.7	12.7	7.8	0.7	0.0	3.1	0.0	0.0	0.0
Ghost or Double Images	94	82	78	32	24	26	6	20	15	2	6	7	2	1	2	0	1	0
	69.1	61.7	60.9	23.5	18.0	20.3	4.4	15.0	11.7	1.5	4.5	5.5	1.5	0.8	1.6	0.0	0.7	0.0

i. Device Failure

There was one device failure reported at one center during the treatment period for this study.

The laser stopped firing during the treatment of a study subject. Although the treatment was completed, VISX field service conducted a thorough evaluation of the system and elected to replace the beam shaping module and hyperopia module at this center. A plastic containing the test ablations was subsequently forwarded to VISX for evaluation. This plastic passed all VISX QA specifications. No other centers reported this problem and no further action was required.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

Preclinical studies completed for this device did not raise any new safety or effectiveness concerns. Clinical studies demonstrated that safety and effectiveness parameters fell within acceptable FDA criteria providing reasonable assurance that the device is safe and effective, when used in accordance with the directions for use, for wavefront-guided LASIK treatment with the VISX STAR S4™ Excimer Laser System with Variable Spot Scanning and WaveScan® derived ablation targets for the correction of hyperopia with and without astigmatism.

XII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

CDRH issued an approval order on 12/14/2004.

The applicant's manufacturing facility was inspected and found to be in compliance with the Quality System Regulation (21CFR 820).

XIV. APPROVAL SPECIFICATIONS

Postapproval Requirements and Restriction: see Approval Order.

Hazard to Health from Use of the Device: see Indications, Contraindications, Warning, Precautions, and Adverse Events in the labeling.

Direction for use: see labeling.